UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,300	05/11/2001	Gregory Ford	STAN177	7800

24353 7590 05/07/2003

BOZICEVIC, FIELD & FRANCIS LLP
200 MIDDLEFIELD RD
SUITE 200
MENLO PARK, CA 94025

EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	15

DATE MAILED: 05/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/854,300	FORD ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-10* is/are pending in the application.

4a) Of the above claim(s) *None* is/are withdrawn from consideration.

5)☒ Claim(s) *1, 3 and 7-10* is/are allowed.

6)☒ Claim(s) *4-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1 and 3-10 are pending.

2. In view of the amendment filed 2/14/03, the following objection remains.

3. Applicant should amend the first line of the specification to reflect the relationship between the instant application and 60/203,513 filed 5/11/00 as stated on the oath. Applicant is reminded that in order for a patent issuing on the instant application to obtain the benefit of priority based on priority under 35 U.S.C. 119(e), a claim for such priority must be made in this application because priority information from application data sheet will not be printed in the patent.

4. The following new grounds of rejection are necessitated by the amendment filed 2/14/03.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 4 and. 6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) an isolated nucleic acid other than a naturally occurring chromosome comprising a sequence encoding the amino acid sequence set forth in of SEQ ID NO: 8 for screening T cell anergy in vitro, (2) the isolated nucleic acid other than a naturally occurring chromosome comprising a sequence encoding the amino acid sequence set forth in of SEQ ID NO: 8 wherein said nucleic acid comprises the nucleotide sequence set forth in SEQ ID NO: 7, (3) an expression cassette comprising the an isolated nucleic acid other than a naturally occurring chromosome comprising a sequence encoding the amino acid sequence set forth in of SEQ ID NO: 8 operatively linked to transcriptional and translational control sequence for the expression of said GRAIL protein, (4) a host cell comprising the expression cassette mentioned above and the cellular progeny of said host cell, (5) a host cell comprising an isolated nucleic acid other than a naturally occurring chromosome comprising a sequence of SEQ ID NO: 7 encoding a GRAIL protein of SEQ ID NO: 8 and the cellular progeny of said host cell, and (6) a method for producing GRAIL protein, said method comprising growth a host cell comprising the expression

cassette mentioned above and the cellular progeny of said host cell whereby said GRAIL protein is expressed, and isolating said GRAIL protein free of other proteins, **does not** reasonably provide enablement for (1) *any* isolated nucleic acid "**comprising**" at least 100 contiguous nucleotide of SEQ ID NO: 7, and (2) *any* isolated nucleic acid that hybridizes under stringent conditions of 50°C or higher and 0.1XSSC (15mM NaCl/0.15 mM Na Citrate) to the nucleic acid sequence of SEQ ID NO: 7 for induction or maintenance of anergy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only five isolated nucleic acid sequences comprising SEQ ID NO: 1 which encodes MRC-OX44 (reference 9.3.1-2), SEQ ID NO: 2 which encodes Nurr2 (reference 19.9.6-3), SEQ ID NO: 3 which encodes lymphtactin (reference 6.5.2-4), SEQ ID NO: 4 which encodes cbl-b (reference A9.5.7-4), SEQ ID NO: 5 which encodes the murine GRAIL of SEQ ID NO: 6 (reference 1-4) and SEQ ID NO: 7 which encodes the human GRAIL of SEQ ID NO: 8 for producing said GRAIL protein. The GRAIL protein is approximately 50kD and migrates as a 3.75K mRNA on Northern. The specification further discloses the polynucleotide encoding GRAIL is used for expressing the GRAIL protein for identifying or detecting the expression of GRAIL in a biological specimen associated with T cell angery in vitro.

The specification does not teach how to make and use *any* isolated nucleic acid mentioned above because the term "comprising" is open-ended. It expands the nucleic acid to include additional nucleotide at either or both ends so long it contains at least 100 nucleotides of the sequence of SEQ ID NO: 7. There is insufficient guidance as to the undisclosed nucleotide to be added and whether the resulting polynucleotide would maintain both structure and function as the claimed polynucleotide of SEQ ID NO: 7. Not only the length of the isolated nucleic acid comprising at least 100 contiguous nucleotides of the sequence of SEQ ID NO: 7 is not disclosed,

there is insufficient guidance and working example demonstrating that any undisclosed nucleic acid of any length would be useful for induction or maintenance of anergy as the full length nucleotide sequence of SEQ ID NO: 7.

Attwood *et al*, of record, teach that protein function is context-dependent and the state of the art of making functional assignments merely on the basis of some degree of similarity between sequences and the current structure prediction methods is unreliable (See figure, entire document). It is known in the art that even single amino acid changes or differences in a protein's amino acid sequence can have dramatic effects on the protein's function. For example, Mikayama *et al* teach that the human glycosylation-inhibiting factor (GIF) protein differs from human macrophage migration inhibitory factor (MIF) by a single amino acid residue (Figure 1 in particular). Yet, Mikayama *et al.* teach further that GIF is unable to carry out the function of MIF and MIF does not demonstrate GIF bioactivity (Abstract in particular). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet *et al* teach that a single Glu to Val substitution in the subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, paragraph bridging columns in particular). Given the lack of guidance as to which changes can be tolerated and relates to its functional usefulness, there is no expectation of success, let alone predicting which undisclosed nucleotide would be useful for screening T cell anergy.

With regard to *any* isolated nucleic acid that hybridizing under "stringent conditions" as recited in claim 6, the claim encompasses any nucleotide sequence of any length which hybridizes to the nucleotide sequence of SEQ ID NO: 7. However, there is insufficient guidance as to the function of any nucleotide that hybridizes to the nucleotide sequence of SEQ ID NO: 7, much less about the structure of the claimed polynucleotide (i.e. the length of the polynucleotide that hybridizes to SEQ ID NO: 7). Further, the specification discloses only exemplary stringent hybridization conditions using the specific probes as set forth in the specification in paragraph 24. Any undisclosed isolated nucleic acid that simply hybridizes to SEQ ID NO: 7 does not mean it will have the same function as SEQ ID NO: 7. Given the indefinite number of undisclosed polynucleotide, it is unpredictable which undisclosed nucleotide that hybridizes to the nucleotide sequence of SEQ ID NO: 7 would be useful for induction or maintenance of anergy.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

7. Claims 4 and 6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* isolated nucleic acid "**comprising**" at least 100 contiguous nucleotide of SEQ ID NO: 7, and (2) *any* isolated nucleic acid that hybridizes under stringent conditions of 50°C or higher and 0.1XSSC (15mM NaCl/0.15 mM Na Citrate) to the nucleic acid sequence of SEQ ID NO: 7 for induction or maintenance of anergy.

The specification discloses only five isolated nucleic acid sequences comprising SEQ ID NO: 1 which encodes MRC-OX44 (reference 9.3.1-2), SEQ ID NO: 2 which encodes Nurr2 (reference 19.9.6-3), SEQ ID NO: 3 which encodes lymphtactin (reference 6.5.2-4), SEQ ID NO: 4 which encodes cbl-b (reference A9.5.7-4), SEQ ID NO: 5 which encodes the murine GRAIL of SEQ ID NO: 6 (reference 1-4) and SEQ ID NO: 7 which encodes the human GRAIL of SEQ ID NO: 8 for producing said GRAIL protein. The GRAIL protein is approximately 50kD and migrates as a 3.75K mRNA on Northern. The specification further discloses the polynucleotide encoding GRAIL is used for expressing the GRAIL protein for identifying or detecting the expression of GRAIL in a biological specimen associated with T cell angery *in vitro*.

With the exception of the specific isolated nucleic acid molecule mentioned above, there is inadequate written description about the *structure* associated with function of *any* isolated nucleic acid "**comprising**" at least 100 contiguous nucleotide of SEQ ID NO: 7 because the term "comprising" is open-ended. It expands the nucleic acid to include additional nucleotide at either

or both ends so long it contains at least 100 nucleotides of the sequence of SEQ ID NO: 7. There is inadequate written description about the undisclosed nucleotide to be added and whether the resulting polynucleotide after additional nucleotide would maintain both structure and function as the claimed polynucleotide of SEQ ID NO: 7.

With regard to claim 6, the claim encompasses any nucleotide sequence of any length, which hybridizes to the nucleotide sequence of SEQ ID NO: 7. There is inadequate written description about the *function* of any nucleotide that hybridizes to the nucleotide sequence of SEQ ID NO: 7, much less about the structure, in turn, the undisclosed nucleotide sequence would be useful for induction or maintenance of anergy. Note, adding functional language to claim 6 would obviate this rejection.

Further, the specification discloses only two polynucleotides such as SEQ ID NO: 5 and 7 encoding human and murine GRAIL, respectively. The specification discloses only exemplary stringent hybridization conditions using the specific probes as set forth in the specification in paragraph 24. Given the lack of a written description of any additional representative species of nucleotide encoding GRAIL, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.* Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

8. Claims 4 and 5 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

The "100 contiguous nucleotides" in Claims 4 and 5 represent a departure from the specification and the claims as originally filed. The specification does not provide a clear support for the said phrase. Applicants have not pointed out the support for the said phrase.

9. The filing date of the instant claims 1, and 3-10 is deemed to be the filing date of instant application because the specification on page 1 has not been amended to reflect the priority claimed to provisional application 60/203,513, filed 5/11/00.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

11. Claims 4-6 are rejected under 35 U.S.C. 102(b) or in the alternative 102(a) (when Applicants amended the first line of specification) as being anticipated by WO 00/25367 publication (Feb 2000, PTO 892).

The WO 00/25367 publication teaches an isolated nucleic acid such as clone HP10574 comprising 2773 contiguous nucleotides wherein the reference nucleic acid sequence has a stretch of 924 nucleotides identical to the claimed sequence of SEQ ID NO: 7, which is at least 100 contiguous nucleotides of the claimed sequence of SEQ ID NO: 7 (See SEQ ID NO: 150 of WO 00/25367 publication, nucleotides from 211-1137 of SEQ ID NO: 150, Claims 2-4 of WO 00/25367 publication, in particular). The reference nucleotide SEQ ID NO: 150 has another stretch of 289 nucleotide identical to the claimed nucleotide of SEQ ID NO: 7, which anticipates the claimed at least 100 contiguous nucleotides (See nucleotides from 1195-1484 of the reference SEQ ID NO: 150, Claims 2-4 of WO 00/25367 publication, in particular). The reference polynucleotide of SEQ ID NO: 150 encodes a protein that is 428 amino acids in length (See reference SEQ ID NO: 130, in particular); the reference amino acid sequence differs from the claimed amino acid sequence set forth in the claimed SEQ ID NO: 8 by only two amino acids (See reference SEQ ID NO: 130, amino acid residues 310 and 313, in particular). The WO 00/25367 publication further teaches isolated nucleic acid that hybridizes under stringent conditions to the claimed nucleic acid sequence of SEQ ID NO: 7 (See 120, Table 33, and caption, in particular). The cDNA fragments and probes disclosed by the WO 00/25367 publication would be expected to hybridize to instant SEQ ID NO: 7 under stringent conditions because the reference cDNA shares 99.1% identity to the claimed nucleic acid sequence. Thus, the reference teachings anticipate the claimed invention.

12. Claims 1, 3 and 7-10 are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

15. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
May 5, 2003

Christina Chan
CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600